UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/651,136	08/28/2003	Sandor Sipka	22740-2	8175

24256 7590 01/29/2008

DINSMORE & SHOHL, LLP
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI, OH 45202

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
01/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/651,136	SIPKA ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-25* is/are pending in the application.

4a) Of the above claim(s) *6-9,11,12,14-16,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,10,13,17-19 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and Declaration by Sandor Sipka under 37 C.F.R. 1.1332 filed on 10/16/2007 are acknowledged.

2. Claims 1-3 and 5-25 are pending.

3. Claims 6-9, 11-12, 14-16 and 20-21 stand withdrawn from further consideration pursuant to 37 C.F.R. 1.142(b) as being drawn to a nonelected species.

4. Claims 1-3, 5, 10, 13, 17-19, 22-24 and newly added claim 25 are currently under examination as they read on a process for inhibiting allergic disease in humans by aerosol administration.

5. The following rejections are necessitated by the amendment filed on 10/16/2007.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 5, 10, 13, 17-19, 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cochran et al. (PTO-892, Reference U) in view of Previte et al. (PTO-892 mailed on 05/16/2007, Reference W).

Cochran et al. teaches:

A. A process for decreasing development of allergic asthma (OVA induced asthma), the process comprising exposing a neonatal or immature mammal (2-3 week old mice) to lipopolysaccharide derived from extracted bacterial endotoxin (E.coli LPS); wherein an infant mammal (2-3 week old mice) is exposed of claim 5; wherein the exposure is achieved by administering an aerosol spray composition (by nasal aspiration) comprising the lipopolysaccharide of claim 10; wherein exposure to the lipopolysaccharide is achieved shortly after birth and during the maturing life cycle of the mammal (exposure at 2-3 weeks of age) of claim 17 (In particular, abstract, page 268, right column, whole document).

B. A process for decreasing inhibiting development of allergic asthma (OVA induced asthma), the process comprising exposing a neonatal or immature mammal (2-3 week old mice) to lipopolysaccharide derived from extracted E. coli bacteria endotoxin of claim 22; wherein the exposure is achieved by administering an aerosol spray composition (by nasal aspiration) comprising the lipopolysaccharide of claim 23 (In particular, abstract, page 268, right column, whole document).

C. A process for decreasing development of allergic asthma(OVA induced asthma), the process comprising exposing a neonatal or immature mammal to lipopolysaccharide derived from extracted bacterial endotoxin (E. coli LPS), and wherein the exposing step comprises administering an aerosol spray composition (by nasal aspiration) of the lipopolysaccharide derived from extracted bacterial endotoxin (E. coli LPS) of claim 25 (In particular, abstract, page 268, right column, whole document).

The claimed invention differs from the prior art by the recitation of:

"irradiation detoxified lipopolysaccharide" in claims 1-3, 5, 10, 13, 17-19, 22-25;

"wherein the irradiation-detoxified lipopolysaccharide is detoxified by exposure of the endotoxin to irradiation at a level of from about 25 to about 150 kGy" in claim 2;

"wherein the irradiation changes the structure of the endotoxin while maintaining its Th1 stimulatory positive immune effect in the resulting irradiation-detoxified lipopolysaccharide" in claim 3;

"wherein a human of 1 month to 2 years of age is exposed" of claims 13 and 24-25;

"wherein exposure to the irradiation-detoxified lipopolysaccharide is achieved on a daily basis during growth of the mammal" of claim 18;

"wherein exposure to the irradiation-detoxified lipopolysaccharide is achieved on a weekly basis during growth of the mammal" of claim 19; and

"wherein a human is exposed" in claim 25

Previte et al. teaches the detoxification of isolated LPS of S. typhimurium, S. enteritidis and E. coli using 4, 4.8 and 4.5 Mrad (about 25 to about 150 kGy) ionizing radiation. The detoxification eliminates lethality induced by its lethal determinants (changes the structure), while retainining antigenticity (maintaining its Th1 stimulatory effect) and pyrogenicity (In particular, abstract, whole document).

The functional limitations of "operable to the Th 1 arm of the mammal' s immune system" in claims 1, 22 and 25 ; and "while reducing interleukin I(IL-1) stimulation caused by the native form of the lipopolysaccharide derived from extracted bacterial endotoxin" of claim 25 are inherent properties of the reference irradiation-detoxified lipopolysaccharide. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir.

1997).

Cochran et al. also teaches that "recent studies raised the intriguing hypothesis that exposure to LPS may interact with the immune system in early life and produce a protective environment against the development of asthma and atopy. Despite the potential importance of this phenomenon in the pathogenesis of childhood asthma, only recently have animal models been used to study the interactions between endotoxin and allergic responses as a function of age" and "patients become symptomatic in their first 5 years of life" (In particular, page 268, left column).Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the process taught by Cochran et al in humans of 1 month to 2 years of age. Cochran et al. suggests performing the process for decreasing development of allergic asthma in young children under 5 years of age implicitly.

Claims 18-19 are included because it would be conventional and within the preview of those skilled in the art to identify and determine the optimal mode of administration. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art would have been motivated to use the irradiation detoxified lipopolysaccharide of Previte et al. in process for decreasing allergic asthma of Cochran et al. because the process should be safe and without toxic effects for use in infants and

children. Previte et al. teaches that LPS can be irradiation-detoxified of its lethal determinants while still retaining antigenicity and pyrogenicity. Therefore, it is obvious to use a safer, less toxic form of LPS in neonatal or immature mammals to decrease allergic asthma.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

8. Claims 1-3, 5, 10, 13, 17-19, 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khan et al. (PTO-892, Reference V) in view of Previte et al. (PTO-892 mailed on 05/16/2007, Reference W).

Khan et al. teaches:

A. A process for decreasing development of allergic asthma (OVA induced asthma), the process comprising exposing a neonatal or immature mammal (3 week old mice) to lipopolysaccharide derived from extracted bacterial endotoxin (LPS); wherein an infant mammal (3 week old mice) is exposed of claim 5; wherein the exposure is achieved by administering an aerosol spray composition (intratracheally) comprising the lipopolysaccharide of claim 10; wherein exposure to the lipopolysaccharide is achieved shortly after birth and during the

maturing life cycle of the mammal (exposure at 3 weeks of age) of claim 17 (In particular, abstract).

B. A process for decreasing inhibiting development of allergic asthma (OVA induced asthma), the process comprising exposing a neonatal or immature mammal (3 week old mice) to lipopolysaccharide derived from extracted E. coli bacteria endotoxin of claim 22; wherein the exposure is achieved by administering an aerosol spray composition (intratracheally) comprising the lipopolysaccharide of claim 23 (In particular, abstract).

C. A process for decreasing development of allergic asthma(OVA induced asthma), the process comprising exposing a neonatal or immature mammal to lipopolysaccharide derived from extracted bacterial endotoxin (LPS), and wherein the exposing step comprises administering an aerosol spray composition (intratracheally) of the lipopolysaccharide derived from extracted bacterial endotoxin (LPS) of claim 25 (In particular, abstract).

The claimed invention differs from the prior art by the recitation of:

"irradiation detoxified lipopolysaccharide" in claims 1-3, 5, 10, 13, 17-19, 22-25;

"wherein the irradiation-detoxified lipopolysaccharide is detoxified by exposure of the endotoxin to irradiation at a level of from about 25 to about 150 kGy" in claim 2;

"wherein the irradiation changes the structure of the endotoxin while maintaining its Th1 stimulatory positive immune effect in the resulting irradiation-detoxified lipopolysaccharide" in claim 3;

"wherein a human of 1 month to 2 years of age is exposed" of claims 13 and 24-25;

"wherein exposure to the irradiation-detoxified lipopolysaccharide is achieved on a daily basis during growth of the mammal" of claim 18;

"wherein exposure to the irradiation-detoxified lipopolysaccharide is achieved on a weekly basis during growth of the mammal" of claim 19; and

"wherein a human is exposed" in claim 25

Previte et al. teaches the detoxification of isolated LPS of S. typhimurium, S. enteritidis and E. coli using 4, 4.8 and 4.5 Mrad (about 25 to about 150 kGy) ionizing radiation. The detoxification eliminates lethality induced by its lethal determinants (changes the structure), while retainining antigenticity (maintaining its Th1 stimulatory effect) and pyrogenicity (In particular, abstract, whole document).

The functional limitations of "operable to the Th 1 arm of the mammal' s immune system" in claims 1, 22 and 25 ; and "while reducing interleukin I(IL-1) stimulation caused by

the native form of the lipopolysaccharide derived from extracted bacterial endotoxin" of claim 25 are inherent properties of the reference irradiation-detoxified lipopolysaccharide. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

Given that Khan et al. teaches "recent evidence has suggested that post-natal exposure to endotoxin may protect against the development of allergen sensitization and asthma"9In particular, abstract), it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the process taught by Khan et al in humans of 1 month to 2 years of age. Khan et al. suggests performing the process for decreasing development of allergic asthma in young post-natal children implicitly.

Claims 18-19 are included because it would be conventional and within the preview of those skilled in the art to identify and determine the optimal mode of administration. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art would have been motivated to use the irradiation detoxified lipopolysaccharide of Previte et al. in process for decreasing allergic asthma of Khan et al. because the process should be safe and without toxic effects for use in infants and children. Previte et al. teaches that LPS can be irradiation-detoxified of its lethal determinants while still retaining antigenicity and pyrogenicity. Therefore, it is obvious to use a safer, less toxic form of LPS in neonatal or immature mammals to decrease allergic asthma.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 10, 2008
Nora M. Rooney, M.S., J.D.
Patent Examiner
Technology Center 1600

Maher M. Haddad
MAHER M. HADDAD
PRIMARY EXAMINER